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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,375	05/10/2005	Yuman Fong	08582/014002	5371
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CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			EXAMINER HAMA, JOANNE	
			ART UNIT 1632	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary

Application No.

10/505,375

Applicant(s)

FONG ET AL.

Examiner

Joanne Hama, Ph.D.

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-13 and 28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-13 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 2, 2007 has been entered.

Claims 2, 14-27 are cancelled. Claims 1, 28 are amended.

Claims 1, 3-13, 28 are under consideration.

Information Disclosure Statement

Applicant filed an Information Disclosure Statement on November 2, 2007. The IDS has been considered.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6, 8-13 remain rejected and claims 3-5, 28 are newly rejected under 35 U.S.C. 102(e) as being anticipated by Fong et al., US 2002/0071832 for reasons of record, December 28, 2005, July 7, 2006, February 12, 2007, and July 24, 2007.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

It is noted that upon further consideration, claims 3-5, 28 are now included in the rejection. Issues as they apply to these claims are addressed as follows. Response to Applicant's rebuttals of November 2, 2007 follows these new grounds of rejection.

As indicated in the Office Action, December 28, 2005, page 5, Fong teaches a method of resecting a tumor from a patient and injecting a virus into the tumor bed to ensure destruction of any remaining tumor cells (page 5). While Fong does not specifically indicate that the method can be used to treat metastasis that is present at a site distal to the site of surgical resection of the tumor in the subject, the method steps of resecting a tumor and then applying lytic virus are the same as those in Fong. Thus, Fong's method steps would have treated metastatic cancer distal to the site of resection and would treat cancer that is present in the lymphatic system of the patient. It is a general rule that merely discovering and claiming a new benefit to an old process

cannot render the process again patentable. In re Woodruff, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); In re Swinehart, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and Ex Parte Novitski, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993).

Applicant's arguments filed November 2, 2007 have been fully considered but they are not persuasive.

Applicant indicates that the subjects treated according to the present invention are subjects in need of treatment of metastasis of cancer at a site distal to the site of surgical resection of a tumor in the subject. Fong does not teach the treatment of such patients. Rather, Fong states that "surgery can be carried out to remove the tumor, and the viruses inoculated into the resected tumor bed to ensure destruction of any remaining tumor cells" (emphasis added). The focus of this passage is the destruction of tumor cells in the tumor bed. Fong does not mention treating metastases at the site distal to the site of tumor resection and treatment according to the method of Fong does not inherently result in the treatment of such metastases (Applicant's response, pages 6-7). Applicant indicates that inherent anticipation is not applicable (Applicant's response, page 7). The patient population treated according to the present invention (subjects in need of treatment of a metastasis at a site distal to the site of surgical resection) is distinct from that treated by Fong. In particular, Fong states that "surgery can be carried out to remove the tumor, and the viruses inoculated into the resected tumor bed to ensure destruction of any remaining tumor cells." The focus of this passage of Fong is thus destruction of tumor cells in the tumor bed. Fong does not

mention treating metastases at sites distal to the site of resection. Further, carrying out the method of Fong would not necessarily result in the treatment of such metastases, as not all tumors would have produced such cells. Therefore, treatment of metastasis at a site distal from the site of surgical resection would not "necessarily flow" from carrying out the method of Fong, and such a result may be considered, at best, to be "occasional," which, as discussed above, is not sufficient to establish inherency (Applicant's response, page 8). In response, this is not persuasive. While Fong may have intended that viruses inoculated into the resected tumor bed to ensure destruction of any remaining tumor cells and was not necessarily indicating (or specifically thinking) that metastatic cells would have also been treated, Fong's method of resecting a tumor and administering virus at the site of resection is would have treated metastatic cancer that was distal to the site of resection whether Fong realized it or not. According to MPEP 2112, II. Inherent Feature Need Not Be Recognized at the Time of the Invention, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. While Fong may be certain that resection and applying virus was intended to rid the tumor site of all cancer cells associated with the tumor, not realizing that the method steps also affected metastatic cancer cells does not have to be realized. In addition to this, while the instant claims are written such that the patient population is those who have metastatic cancer, Fong's teaching is not exclusive such that the method disclosed was specific for patients who do not have metastatic cancer. Rather, Fong teaches treatment of cancer, which includes patients with

metastatic cancer. In addition to this issue, it is noted that the method steps of Fong is the same as that of the claims: resecting a tumor and administering oncolytic virus. Because the method steps are the same between the claims and the Fong publication, Fong anticipates the claimed invention.

In response to Applicants' prior submission concerning the fact that intraperitoneal administration was used with respect to the example in Fong concerning OCUM-2MD3 cells, the Examiner makes note of paragraph 36 of the Fong publication, where administration to a surgical bed is suggested, as discussed above, and states that the example was viewed in consideration of whether Fong had support for the general method described on page 5. In response, Applicants submit that the OCUM-2MD3 passage does not support the cited passage of paragraph 36, as different modes of administration (intraperitoneal vs. inoculation into a resected tumor bed) are used (Applicant's response, page 8). In response, Applicant's response that the OCUM-2MD3 passage does not support the cited passage of paragraph 36 is persuasive as different modes of administration are used. However, Applicant's response does not overcome the rejection at hand with regard to the claimed method being anticipated as Fong teaches resection and administration of oncolytic virus to the site of resection.

With regard to the Examiner indicating "the phrase 'treating metastasis' is broad and in addition to ablating distant sites of cancer, 'treating' could also mean 'preventing' metastasis." Applicants respectfully disagree with this characterization of these terms. In particular, in order for something to be treated, it must exist. Thus, use of the word "treating" in claim 1 shows that the metastasis that is subject of the treatment exists as

a metastasis and is not a potential metastasis as represented by an as-of-yet unmetastasized cell in a tumor bed. In the interest of expediting prosecution, Applicants note that claims 1 and 28 have been amended to specify that the treated metastasis "exists at a site distal to the site of surgical resection." In response, Applicant's amendment in claim 1 clarifies that metastatic cancer be present when "treating metastasis" and is not readable on prevention of metastasis. While Applicant makes the amendment to specifically indicate that the patients to be treated by the claimed method have metastasis, Fong anticipates the claims because Fong discloses the claimed method steps, regardless of whether there was intent to treat metastatic cells.

Thus, the claims are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 6, 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fong et al., US 2002/0071832 in view of Wong et al., 2001, Human Gene Therapy, 12: 253-265, for reasons of record, December 28, 2005, July 7, 2006, February 12, 2007, July 24, 2007.

Applicant's arguments filed November 2, 2007 have been fully considered but they are not persuasive.

Applicant indicates that the Examiner makes note of the anticipation rejection based on Fong, stating that the Fong method includes the same steps as those of the present claims. As discussed above, Fong does not anticipate the present claims, as carrying out the method of Fong does not necessarily result in the method of the present invention (Applicant's response, page 10). In response, the method of Fong does result in the method of the present invention because Fong's teaching is applicable to cancer patients regardless if they had metastatic cancer or not. While Fong intended in the method to rid the resection site of cancer and was not necessarily expecting that the treatment would have treated metastatic cells, the steps of Fong are the same as the claims and the method would have treated metastatic cells distal to the site of resection.

With regard to the Examiner stating that claim 1 is not specific for patients with lymphatic metastatic cancer, Applicants respectfully submit that it was not known that virus administered to a surgical bed could travel from the site of the surgical bed by any means (including via the lymphatic system). Thus, as this general concept was not known, Fong does not provide any suggestion or motivation to carry out the presently claimed invention. Applicant also indicates that a suggestion or motivation to carry out the claimed invention also does not come from Wong, which was cited as describing a particular attenuated, replication-competent, oncolytic herpes simplex virus, NV 1023. (Applicant's response, page 10). In response, as indicated in MPEP 2112, whether or not Fong realized that the method of resecting a tumor and administering oncolytic virus at the site treats metastatic cancer that is distal to the resection site, the method steps

are the same and would have treated cancer patients that have metastatic cancer.

With regard to administration of NV 1023, Wong et al. teach that NV 1023 can be used to treat cancer and thus, an artisan would have been motivated to use NV 1023 with the method of Fong et al.

As such, the claims remain rejected.

Claims 1, 3-6, 8, 9, 28 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kooby et al., 1999, FASEB J. 13: 1325-1334, in view of Rodgers and McCall, 2000, British Journal of Surgery, 87: 1142-1155, for reasons of record, February 12, 2007, July 24, 2007.

Applicant's arguments filed November 2, 2007 have been fully considered but they are not persuasive.

Applicant indicates that there is no teaching or suggestion in these references, that administration of virus using the method of Kooby would even reach the hepatic lymph nodes. In particular, portal infusion of Kooby involves administration via the portal vein (see page 1327), while hepatic lymph nodes are located in mesenteric tissue, along the hepatic artery. As stated in Applicants' prior reply, when mentioning the possibility of using their approach in conjunction with surgical resection, Kooby notes that the treatment is to reduce local recurrence. This is shown, for example, at page 1332 in Kooby. Kooby provides no motivation or suggestion to treat metastases to hepatic lymph nodes, and such motivation or suggestion is also not provided by Rodgers. Before the present invention, it simply was not known that administered virus

can travel from a site of resection. Thus, there would have been no motivation, based on Kooby, for this to be carried out (Applicant's response, page 11). In response, the rejection was written because an artisan would have arrived at the claimed invention, using the teachings of Kooby et al., in view of Rodgers et al. Motivation of combining two types of tumor therapy (resection and lytic virus) was provided by Kooby et al. Kooby et al., in view of Rodgers et al. renders the claims obvious for the two required steps of the claimed method. Applicant indicates that nothing in Kooby et al. or Rodgers et al. teach that administration of virus would even reach the hepatic lymph nodes. In response, there is no requirement that Kooby et al. nor Rodgers et al. teach treatment of hepatic lymph nodes. The claims as written require that a tumor be resected and that oncolytic virus be administered to the resected site. Kooby et al. and Rodgers et al. provide this teaching. Whether or not the art at the time of filing realized the unknown benefit of treating metastatic cancer in lymph nodes is not necessary to show obviousness. See MPEP 2112.

Applicant indicates that even though Rodgers teaches that colorectal cancer can have metastases in hepatic lymph nodes, there is no basis in either of the cited references or the art in general that metastases could be treated using a method such as that taught by Kooby. Rather, as noted above, the method of Kooby, when applied in the context of surgical resection, was done to reduce local occurrence. A patient treated using such a method may have metastases in many other places, including hepatic lymph nodes, but there is no teaching or suggestion in the cited references (or in the art in general) that any such metastases could be treated using the method of the

Kooby (Applicant's response, pages 11-12). In response, while Applicant indicates that Kooby et al. is applied in the context of surgical resection to reduce local occurrence, demonstrating obviousness of the claim does not require that treating metastatic cancer in lymph nodes was required to be known. Again, referring to MPEP 2112, an artisan need not know that there are inherent properties of the claimed invention. As discussed above, all that is required to make the claims obvious is that the art needs to show that the two steps of resection and administration of virus be known and have a rationale to be combined. Kooby et al. provide motivation of combining two types of cancer therapy. As such, the claims are obvious.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Joanne Hama
Art Unit 1632

